REMARKS

Favorable reconsideration of the subject application is respectfully requested in view of the above amendments and the following remarks. This Amendment and Reply, which accompanies a Request for Continuing Examination (RCE), is responsive to the final Office Action mailed April 12, 2005. ***Applicants note that this application has been granted Special Status and respectfully request that the Examiner expedite her review of this Amendment and Reply.***

Independent claim 32 has been amended to delete language that was previously deemed to be indefinite and to add language specifying that the antiseptic composition is packaged in a sterile, pyrogen-free form. This subject matter was previously recited in dependent claim 44. Claim 44 has consequently been amended to remove the dependency from claim 32.

Claims 32, 37, 39, 42, 45, 55 and 56 have been amended to replace the terminology "solvent" with "solution." The "solution" terminology is perceived to provide clarification and no substantive change is intended by this amendment. Both terms are used in applicants' specification without any intended distinction in their meaning.

Claims 40 and 54 have been cancelled without acquiescing in the outstanding rejections and without prejudice to applicants' ability to present these claims or similar claims in the future. The dependency of claims 34, 37, 39, 42, 44, 45, 46 and 47 has been amended to delete reference to claim 54.

Independent claim 55 has been amended to specify that the solution is water. This subject matter is described throughout the application as filed, for example, at page 15, line 10; page 19, line 31; and page 21, line 36.

Independent claim 56 has been amended to delete reference to the lock flush composition being "safe," which was deemed to be indefinite, and to specify that the lock flush composition is packaged in a sterile, pyrogen-free form. This subject matter is recited in claim 44, which was previously dependent on claim 56. Claim 44 has consequently been amended to remove the dependency on claim 56.

Claim 57 has been added to combine the subject matter of dependent claim 34 and independent claim 32. The dependency of claim 32 has consequently been amended and claims

37, 39, 41, 42 and 45-57 have been amended to additionally depend from new independent claim 57.

Claims 32, 34, 37, 39, 41, 42, 44-47, and 55-57 are pending, with claims 32, 54, 56 and 57 being in independent claim format.

Claim Objections

The Examiner objected to Claim 56 because the term "in" in line 5 of the claim is used twice. This is not in error. The term "in-dwelling access catheters" is a term of art that means access catheters that are permanently or semi-permanently installed in a patient. Applicants' claimed lock flush compositions are biocompatible for use in such (in-dwelling) permanently or semi-permanently installed devices. Applicants submit that correction is not required.

The Examiner also objected that claims 34, 37, 39, 40, 42, 44, 45, 46 and 47 depend on higher-numbered claims such as 54, 55 and 56. This is necessary since newly added claims must be numbered consecutively from the previously added and considered claims. Prior to issuance, the claims will be renumbered. Applicants submit that correction is not required.

Claim Rejections – 35 USC §112

The word "safe" in claims 32 and 56 was deemed vague and subjective. Claims 32 and 56, and the claims dependent thereon, were consequently rejected for failing to particularly point out and distinctly claim the subject matter of applicants' invention. Applicants do not acquiesce in this rejection but, for purposes of expediting prosecution and allowance of the pending claims, have eliminated the word "safe" from claims 32 and 56.

The word "modest" in claim 32 was deemed to be a relative term that rendered the claim indefinite. Claims 32 and the claims dependent thereon were consequently rejected for failing to particularly point out and distinctly claim the subject matter of applicants' invention. Applicants do not acquiesce in this rejection but, for purposes of expediting prosecution and allowance of the pending claims, have eliminated the word "modest" from claim 32.

Claim 40 was rejected on the basis of its use of the term "substantially" and for its use of the term "agent." Without acquiescing in this rejection and without prejudicing applicants' ability to prosecute this or similar claims in another application, claim 40 has been cancelled.

Applicants submit that the pending claims particularly point out and distinctly claim the subject matter of applicants' invention and fully satisfy the requirements of 35 U.S.C. §112.

Claim Rejections – 35 U.S.C. §102(b)

Claims 32, 34, 37, 40-42, 45 and 54-56 were finally rejected under 35 U.S.C. §102(b) as being anticipated by *Kurginski* (GB 1 279 148). Applicants specifically do not acquiesce in this prior art rejection and have presented amended claims to expedite prosecution and allowance of claims rather than to correct deficiencies in the previously pending claims.

Applicants' independent claims 32, 55 and 56 have been amended to introduce additional subject matter or to provide clarification and thereby, it is believed, remove *Kurginski* from consideration as a 102(b) anticipating reference. Specifically, the Examiner notes that *Kurginski* fails to recite: (i) a saline carrier for the EDTA injection; (ii) employment of the composition in a sterile, pyrogen-free form; and (iii) employment of the composition in a sterile condition in a pre-filled syringe. Independent claims 32 and 56 specify that the antiseptic composition (claim 32) and the lock flush composition (claim 56) are packaged in a sterile, pyrogen-free form. Dependent claims 39 and 46, respectively, provide that compositions of the present invention comprise a saline carrier and are in a sterile condition in a pre-filled syringe. In light of the outstanding final rejection, it is believed that independent claims 32 and 56, as presently amended, would be subject to the obviousness rejection of claim 44 – that is, claims 32 and 56 would allegedly be obvious in view of *Kurginski* and *Remington's Pharmaceutical Sciences*.

Kurginski discloses an industrial cleaning solution for use in the sanitary maintenance of toilet facilities. The *Kurginski* composition is provided at a pH of from 7 to 12 and comprises a chelating agent, which may be tetra-sodium EDTA, and a solvent admixture including a loweralkanol of from 1 to 4 carbon atoms, an alkanolamine of which any alkanol moiety is of from 2 to 4 carbon atoms, with from 1 to 3 such alkanol moieties per molecule, a mixture of two or more different loweralkyl ether alcohols of which each is terminated on one end by an alkyl group of from 1 to 4 carbon atoms, either bonded through oxygen to an alkylene moiety of from 2 to 4 carbon atoms, the alkylene moiety being terminated by a hydroxyl group, and water.

Independent claim 55 has been amended to specify that the solution component of applicants' claimed antiseptic composition is water. *Kurginski* teaches solutions wherein the

solvent is an admixture of several organic constituents (enumerated above) and water. The Kurginski composition described in Example 1, for example, includes a solvent admixture of methanol, diethanolamine, 2-butoxyethanol, 1-methoxy-2-propanol and de-ionized water. Although water is the highest percentage constituent in the liquid composition, applicants perceive no teaching or suggestion in *Kurginski* of a composition comprising a different solvent admixture or fewer solvent components or of a composition in which the solution is water.

Another liquid cleaner is described in European patent publication number 0 171 122 A1, which was cited recently in a corresponding PCT International Search Report and is cited in the accompanying Supplemental Information Disclosure Statement (IDS). A copy of this publication is being provided with the IDS. This publication describes liquid hard surface cleaners with "excellent cleaning properties and high 'shine' quality" formulated at a pH range of 9.5 – 11 and comprising at least EDTA (preferably tetra-sodium), benzylalcohol and water. Other constituents may be added. The benzylalcohol constituent is described as the "primary cleaning ingredient." Applicants perceive no teaching or suggestion in this reference of a composition in which the primary cleaning ingredient is omitted and the solution is water.

It is urged that applicants' amended independent claim 55, and the claims dependent therefrom, are not anticipated by or obvious in view of either of these references or any other references of record.

Claim rejections – 35 U.S.C. §103

As noted above, independent claims 32 and 56, as amended herein, and newly added claim 57, specify that the antiseptic composition (claims 32 and 57) and the lock flush composition (claim 56) are packaged in a sterile, pyrogen-free form. Dependent claims 34, 37, 39, 40, 42, 44, 46 and 47 introduce additional subject matter. We will discuss these claims with reference to the combination of *Kurginski* and *Remington's Pharmaceutical Sciences* and/or *Root et al.*

Kurginski teaches a cleaning composition for releasing the particular soils that tend to accumulate in toilets and similar sanitary facilities. (*See*, page 1, lines 12-15). Three types of "soils" are problematic in the management of sanitary facilities and are effectively removed by the *Kurginski* cleaning composition: (1) mineral-like deposits that accumulate on and adhere to

toilet surfaces (*See*, page 1, lines 22-48); (2) closely adherent fecal matter (*See*, page 1, lines 49-57); and (3) rust (*See*, page 1, lines 58-62). These soils may provide a site for bacterial and fungal growth (*See,* page 1, lines 60-62) and the growth of the microorganisms over a period of several weeks may constitute another soil problem. As noted by the Examiner in her comments in the Advisory Action, the composition of *Kurginski* solubilizes the hard deposits, as well as gelatinous microorganisms (*See,* page 2, lines 5-10). Applicants note that "solubilizing" gelatinous microorganisms is quite distinct from producing a bactericidal effect and it is clear that *Kurginski* does *not* teach that its compositions have a bactericidal effect. To the contrary, *Kurginski* teaches that, when desired, a germicide may be added to the composition to disinfect or sterilize surfaces (*See*, page 3, lines 74-76).

Remington's Pharmaceutical Sciences discloses sterile, pyrogen-free solutions of sodium chloride for injection, usually intravenously. It also discloses that syringes are "instruments intended for injection of liquids into the body or its cavities." Various types and sizes of syringes are described. Hypodermic syringes, for example, are used to administer medication subcutaneously or intradermally, intravenously or intramuscularly. Applicants agree that hypodermic syringes are well known and that sterile, pyrogen-free solutions, including saline solutions, are conventionally used for human and animal therapeutic or diagnostic injections.

This does not, however, lead to the conclusion that it would be obvious to formulate any compositions, including applicants' claimed compositions, in a sterile, pyrogen-free form. If applicants' claimed compositions were known or suggested to have therapeutic or diagnostic applications, their formulation in a sterile, pyrogen-free form would certainly be obvious. The prior art relied upon for rejection, *Kurginski*, teaches that its composition, which may comprise tetra-sodium EDTA at a concentration and pH that overlaps the concentrations and pH ranges specified by applicants, is a toilet cleaner. The additional prior art reference cited in the accompanying Information Disclosure Statement, European patent publication 0 171 122 A1, discloses tetra-sodium EDTA in liquid cleaner compositions comprising benzylalcohol as a primary cleaning ingredient for industrial hard surface cleaning and shining applications. It is inconceivable that either of these compositions would be contemplated for injection into a person or animal and that it would consequently be obvious to formulate such a composition in a sterile, pyrogen-free form.

It was not until applicants made the unexpected and very fortuitous discovery that solutions comprising tetra-sodium EDTA at the concentrations and pH specified in applicants' have a bactericidal effect over a broad spectrum of microbes that there was any reason or motivation to package such solutions in a sterile, pyrogen-free form, or to package such compositions in a pre-filled syringe or a single-dosage vial. Applicants note that their compositions aren't packaged in a sterile, pyrogen-free form for purposes of injection, but rather because they're used in connection with devices or surfaces that are in close proximity to internal bodily fluids or other devices and surfaces that must be maintained in an antiseptic condition to prevent infection.

The previous Examiner argued in the final rejection that it would have been obvious to a person of ordinary skill in the art to be motivated to employ the claimed compositions without pyrogens, and with a carrier such as saline solutions *as is conventional with therapeutic regimen*, and with conventional sterile protocols. The Examiner stated, in the Advisory Action, that it is obvious to a person of ordinary skill in the art at the time the invention was made to store the compositions in a sterile condition and administer using prefilled syringes as taught by *Remington Pharmaceutical Sciences*. Applicants strenuously disagree. It is certainly not obvious to store every composition in a sterile condition or to administer every composition using a prefilled syringe. If compositions have known or suggested application(s) as therapeutic or diagnostic agents, the teachings of *Remington Pharmaceutical Sciences* may be pertinent and may supply the needed teaching or motivation. At the time applicants' invention was made, however, the prior art of record indicates there were two known applications for compositions comprising tetra-sodium EDTA at applicants' claimed concentration and pH ranges: toilet and sanitary facility cleaning (*Kurginski*) and hard surface cleaners and shiners (EP 0 171 122 A1).

It is simply not obvious to provide compositions having these applications in a sterile condition, or to provide such compositions in pre-filled syringes or single-dosage vials. Absent applicants' discovery and teachings, it was unknown that the claimed compositions were useful in connection with any human health purpose or any therapeutic or diagnostic regimen. One of ordinary skill in the art would certainly *not* have been led or motivated to prepare or use the claimed compositions in a conventional sterile therapeutic or diagnostic manner by any teachings

of *Kurginski* and there is no suggestion in either *Kurginski* or *Remington Pharmaceutical Sciences* for any such combination.

Applicants' claim 47, reciting the claimed compositions in a single-dosage vial, was rejected additionally in view of *Root et al.*, which discloses the use of di-sodium EDTA solutions in connection with experiments to determine the inhibitory effect of di-sodium EDTA upon the growth of *Staphylococcus epidermidis* in vitro and the relation to infection prophylaxis of Hickman catheters. This rejection is respectfully traversed. *Root et al.* does not overcome the deficiencies of *Kurginski* and *Remington Pharmaceutical Sciences* with respect to applicants' independent claims.

The *Root et al.* compositions, the experimental model, the data presented and the conclusions drawn, are specifically *based upon **disodium EDTA*** [See Col. 1, paragraph 3]. Applicants' claimed compositions are specifically directed to ***tri-sodium and tetra-sodium EDTA*** solutions having specified concentrations and a specified pH. As noted in applicants' specification at the paragraph spanning pages 13 and 14, the British Pharmacopoeia (BP) specifies that a 5% solution of di-sodium EDTA has a pH of 4.0 to 5.5. Root et al.'s di-sodium EDTA compositions not only have substantially different pH properties, but they have substantially different bactericidal properties, as evidenced by applicants' experimental data presented in Example 1 and illustrated in Figs. 1A – 1C. Root et al. does not render applicants' claimed compositions obvious, either alone or in combination with *Kurginski* and/or *Remington Pharmaceutical Sciences*.

The Examiner has not and cannot establish a *prima facie* case of obviousness based on the prior art references relied upon for rejection or any other prior art references of record. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. MPEP §2143. The mere fact that references *can* be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *Id.* Applicants submit that the Examiner has not established a *prima facie* case of obviousness.

It is respectfully submitted that applicants' independent claims and the claims dependent therefrom are not obvious in the manner required by 35 U.S.C. §103.

Conclusion

Applicants urge that the pending claims are in allowable form. Early reconsideration and allowance of applicants' pending claims is respectfully requested.

Respectfully submitted,

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